ON THE

PROGRESS OF NEUROLOGY.

BY

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Mr. President and Gentlemen:—When invited by the President of this Association to deliver a lecture before its members upon some subject pertaining to the nervous system, I must confess that, while I appreciated deeply the honor conferred upon me, the prospect was associated with a certain degree of anxiety and trepidation. Unless a man is confident that what he has to say to an audience composed in large part of busy practitioners, will interest and encourage as well as instruct his hearers, I can conceive of no possible excuse which could justify his appearance before them. On turning the matter over in my mind, however, it seemed to me that to a body of men so interested in the more purely scientific side of our profession that they support and attend each year a course of lectures upon scientific subjects related to medicine, a brief review of the methods which have been and are being employed in neurological investigation, together with an epitome of the main results thus far achieved from their application, could scarcely fail to be entertaining and helpful.

Indeed, on further consideration, and especially in the attempt to arrange the available matter in a more or less orderly fashion, it has struck me that the marked technical progress made and the enormous widening of knowledge concerning structure

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and function with regard to the nervous system more than any other part of the human or animal body are peculiarly fitted to arouse enthusiasm and compel the admiration of the practical man.

In the brief time at my disposal it would be folly to attempt any minute description of technical methods or any laborious analysis of the details of individual original investigations. Such circumstantialities find a suitable repository in the special journals and reference volumes, not in a general lecture. I shall rather attempt, therefore, to indicate as succinctly as possible the broad lines of development and expansion of neurological technique, to point out the relation of modifications of old and inventions of new methods to the successive discoveries in neural morphology and physiology, and, possibly, to make some references to the probable lines of advance in the future. In the course of my remarks I shall have something to say with regard to the combination of instruction with investigation in the study of the nervous system, the importance of division of labor and co-operative activity, and the desirability of the association of well organized laboratories in which anatomical and physiological researches are undertaken with well-equipped hospitals and asylums manned with clinicians thoroughly trained in the modern methods of investigating disease.

It will be simplest to begin by a glance at the conception of structure and function entertained by investigators at present, and afterwards to consider briefly some of the methods by which this conception has been gained.

The human individual as a member of modern society and the product of civilization is an animal manifesting physiological activities more complex and diversified than those of any other member of the animal series, and far more intricate and varied than those of the primitive tribes still to be met with in certain parts of the world. Between the most complex of animals and the simplest Protozoan species extends a series of organisms representing a scale of complexity of form and function most delicately graded. Common to every member of the series, though varying in constitution, is the substance which for want of a better name we call protoplasm. Equally common throughout the animal kingdom are certain fundamental activities—the capacity to assimilate food stuffs, to get rid of excrementitious products, to react to stimuli emanating from the environment, to give rise to other organisms of the same kind. As every one knows, however, the amount of protoplasm and the way in which it is distributed varies enor-

mously in different animals; it is also a matter of every day experience that the fundamental properties of protoplasm are by no means identical in their manifestations in the different species of organisms. Morphological differences are constantly correlated with physiological distinctions. In the lowest forms of animals the protoplasm exists as a simple continuous mass—a cell—containing within it certain more differentiated and apparently more solid masses—the so-called nucleus, centrosome and archiplasm. In all higher animals the protoplasm, at the beginning of the animal's life, is also met with in the form of a continuous mass, the fertilized ovum, a single cell, containing within it, nucleus, centrosome and archiplasm; this unicellular condition does not, however, last long, for by a repeated process of division the single protoplasmic mass becomes broken up into, first, two cells, then four, then eight, and so on until ultimately in an animal like man, according to the estimate of Francke, there are as many as 26½ billions of cells. The original relatively simple minute microscopic lump of protoplasm has by assimilation of suitable food under favorable conditions grown into a manifoldly divided mass of protoplasm and protoplasmic derivatives weighing say 150 pounds or more. I shall not stop to discuss the factors, external and internal, which are operative in this gradual process of protoplasmic growth and subdivision, interesting as such a discussion could be made, but shall simply remind you that as the subdivision proceeds groups of the masses which result begin to exhibit structural peculiarities which distinguish them from one another, and which are markedly different from those of the common mother-cell.

The body, as we are accustomed to say, becomes differentiated into a number of groups of cells—the cells of the individual groups resembling one another closely, but differing strikingly in microscopical appearance from those of other groups. As a result of this manifold subdivision of the living substance, certain of the cells have come to be in more intimate contact with the external world than others, some are closer to the supply of crude food, some are exposed directly to light and air, etc. Cavities form, intercellular substances, solid and fluid, are manufactured and the organism is now a multicellular mass, of which the individual cells or individualities of a lower order are so related to one another and so co-ordinated in their activities that the whole animal appears to act as a unit—is indeed a unit or individuality of a higher order. The life of the higher unit "is not, however, an indivisible unitary archeus

dominating, from its central seat, the parts of the organism, but a compound result of the synthesis of the separate lives of those parts," i. e. of the separate lives of the organic individualities of a lower order.

The cells of a higher organism, though individuals, are not, in a sense, as independent as are free unicellular organisms. They represent, on the contrary, individual members of a great cell-state, in which the principle of physiological division of labor holds, and in which each individual to a greater or less extent affects and is in turn affected by every other individual of the billions which constitute the state. The reciprocal influences vary enormously according to the position and nature of the individual cells; some cells touch one another, some are directly united with adjacent cells by means of protoplasmic bridges, others are brought into relation with widely distant cells by means of extremely long protoplasmic processes or with the help of delicate fibrils the product of the activity of the protoplasm of the cells; while through the lymph and blood, which can carry chemical substances in solution, every cell is placed in a position to act upon or to be acted upon by any other cell in the body.

Though in the physiological division of labor each of the individualities of the lower order sacrifices in a certain degree its independence, yet it is in this way alone that it is possible for it to attain to a specialization of function, and had it to care for all the exigencies of the life of an independent isolated organism it could not long continue its existence in its peculiar condition. It is only by virtue of its membership in a well-organized state composed of a multitude of individuals divided into groups of workers of various sorts that it can with safety follow, as it were, "its own bent" and attain to a high degree of perfection in its own specialized physiological activity. The whole multicellular organism, on the other hand, can maintain a normal existence only when each individual group of workers functions in its proper time, place and intensity so that the sum total of the activities of the various specialized group of workers is just sufficient for the "continuous adjustment of the internal to the external relations" of the organism; in other words, all goes well only so long as the activities of the various parts maintain collectively a certain equilibrium.

But it is not to be thought that in the differentiation of the multicellular organism into organs and tissues, each cell in developing a special function loses entirely the general fundamental properties of protoplasm; on the contrary, each of the

specialized individualities retains the power to assimilate food, to give off excrementitious substances and often the capacity of reproducing its like; the difference in capacity is one of degree rather than of kind. The specialized cell may not be capable of digesting crude food stuffs; it may require that its nutriment be especially prepared for it by other cells or even by a whole series of other cells of different varieties. Again, the excrementitious products of a specialized cell may not consist of substances that can be directly eliminated by the body; very often doubtless other cells have to carry the process of combustion and analysis further; indeed, the excrementitious product of the former cell may constitute a suitable article of diet for the latter.

The various groups of cells in the human body so curiously differentiated morphologically in correspondence with their specific physiological activities are already well known to all of you. The great group of cells of hypoblastic origin have been set apart for purposes of digestion and respiration; they build zymogens, acids and alkalies and pour them out into the alimentary canal, where they mix with the food and prepare parts of it for absorption and utilization by the other cells of the body, or, as in the lungs, they mediate the gas-interchange between the air in the pulmonary alveoli in contact with their distal surfaces and the corpuscles and fluids of the blood situated proximal to them. The mesoblastic cells build intercellular substances and form the framework of the body upon which the soft parts are hung. Some of the intercellular substances become calcified and in the form of bone supply "struts and ties for the bearing of thrusts and tensions;" in other instances the intercellular substances are firm but elastic and supply the resilient material suitable for the articular surfaces of joints. Other mesoblastic cells build fibres of various sorts—long, tough, non-extensile fibrils as in tendon, aponeurosis, and ligament—elastic fibrils as in areolar tissue or the extremely delicate mesh-work of finest fibrils such as those met with in the fine meshed reticulum supporting the parenchymatous elements of the various organs. In the muscle cells we see the embodiment of a special function of high dignity—contractility. In the protoplasm of these cells are laid down certain longitudinal structures—plasma products—which look like fibrils often with curious cross-markings—structures which are undoubtedly associated in some way, though we are yet ignorant how, with the approximation of the two ends of the fibre when the latter is stimulated. The cells of ectoblastic origin become divided into

various groups, some of them forming a superficial covering for the body and certain appendages of that covering as hair and nails, others entering the orifices to provide them with a lining, still others dipping down beneath the surface to build the secreting glands which elaborate the milk, the sweat and the sebum.

A very large proportion of the ectoblastic cells—brothers or sisters of the epidermal cells—become especially differentiated along the lines of irritability and response and go to form the central nervous system, the axis cylinders of the peripheral nerves, and the true nervous elements of the various sense-organs.

The nervous system, as we know it to-day, consists like all the other tissues of the body of an aggregation of cells and of intercellular substances derived from the cells. Aside from the covering membranes and the blood vessels with the tissue immediately surrounding them in the central nervous system, and the connective tissue, blood and lymph vessels and neurilemma sheaths of the peripheral nervous system, all the cellular elements and intercellular substances of the nervous tissues are believed to be derived from this ectoderm or outermost of the three layers of which the embryo is composed at an early stage.

These cells and intercellular substances of ectoblastic origin in the nervous system may be divided into two great classes: (1) that including the true nerve cells and their derivatives, and (2) that including all the other cells in the central nervous system and their derivatives, namely, the elements classed as neuroglia and ependyma. Thanks to the newer investigations the form relations to be met with in connection with these two groups are gradually being unravelled, and it is to an epitome of our knowledge concerning these that I wish to direct your attention particularly this evening.

One of the most striking differences between a nerve cell and most other cells of the body is the curious distribution in space of parts of the protoplasm composing it; while a subdivision of the peripheral parts of the protoplasmic mass with formation of cell processes does occur in several tissues of the body, nowhere else is this subdivison so pronounced, nowhere are cell processes so long, so complex, and so manifoldly branched and so ultimately delicate as in the nervous system. Indeed, for a long time these intricate subdivisions of processes and many of the very long delicate processes were not known to constitute integral parts of nerve cells, and it was not until

they became recognized as such that the cell doctrine could be satisfactorily applied in the nervous system. To distinguish the whole nerve cell, inclusive of all its processes from the torso recognized by the older observers as the nerve cell, Waldeyer has introduced the term *neurone*, a designation which has met with almost general adoption. While I shall speak of the specialized cell-individuals in the nervous system as neurones, I do not mean to imply that we meet here with structures incomparable to other cells in the body; on the contrary, the neurones or complete nerve cells are individualities of a lower order quite comparable with other individualities of the same order, e. g. with gland cells, smooth muscle cells, tendon cells and the like. In the case of the neurones, the special labor performed has to do with the functions of irritablity and conductivity; in the gland cell the most manifest functional capacity is secretion; in the muscle cell, contractility; in the tendon cell, the manufacture and nutrition of firm fibrils for mechanical purposes. In every instance we may assume that the structural peculiarities met with correspond to the physiological functions to be performed, although as yet we may be unable to correlate all the details of structure with their corresponding details of function.

Nearly all the nerve cells or neurones possess more than one process; indeed, in most there are many processes, though in some cells only two exist. In the cells with many processes the latter are found as a rule to consist of two sorts: (1) much branched processes never extending to very great distances from the main mass of protoplasm of the cell, processes which come off by a rather thick wedge of origin from the main protoplasmic mass, branch manifoldly soon after leaving the cell and soon exhaust themselves by multiple division, and (2) longer slender processes, each one arising from the principal protoplasmic mass by a narrow wedge of origin and extending for a shorter or longer distance, maintaining or nearly maintaining its original calibre on the way and giving off in its course only a few delicate side fibrils or collaterals. Ultimately it, like each of the side fibrils, divides several times and exhausts itself in delicate terminal arborizations — the so-called telodendrions. To the first set of processes, usually multiple, the term "dendrites" is applied; to the second set of processes usually, however, single for one nerve-cell, the name "axones" has been given. That there are neurones free from dendrites, and that there are others entirely devoid of axones need not detain us here, nor need we at this time con-

sider the elaborate nomenclatures which have been introduced for convenience of description of certain peculiarities of number, distribution and function of neurones in various parts. One important point, however, must be mentioned, viz., the axones of the various neurones differ enormously in length. Thus, whereas some axones are very short, extending for perhaps only a few millimetres, or even for a fraction of one millimetre from the cell-body, others are much longer, extending even to many centimetres, and in extreme instances for a distance greater than half the whole length of the human body. The neurones with long axones have been called by Golgi cells of Type I, and those with short axones cells of Type II. They are, perhaps, better designated with von Lenhossék as inaxones and dendraxones. The classification is merely a matter of convenience, since transitional forms exist. It is interesting to note that the long axones become surrounded during development by a myelin sheath, while the short axones are not thus enveloped. Outside the central nervous system, the axones of the cerebrospinal neurones are surrounded, not only by a myelin sheath, but also by a cellular sheath, the neurilemma, while the sympathetic axones are devoid of myelin sheaths, but retain a partial cellular covering. The axis cylinder of every nerve fibre is in reality but the axone of some neurone, that is, a long drawn out process of the protoplasm of a nerve cell. The perikaryon of a neurone, that is, the main protoplasmic mass containing the nucleus and its dendrites, does not become surrounded by myelin sheaths, but, in certain instances, at any rate are enclosed in an external reticular covering of peculiar structure, resembling, as has been suggested, a stocking drawn over the protoplasmic mass.

The main mass of protoplasm or perikaryon with its contents, together with all its dendrites and their subdivisions, the axone with its side fibrils, collaterals and end ramifications constitute, then, a single nerve cell, or neurone, that is, the particular form of individuality of the lower order met with in nervous tissues. It is estimated by Donaldson, of Chicago, that of the 26½ billions of cells in the human body, some three thousand millions are nerve cells, an estimate which, as I have suggested elsewhere, if, of necessity, not quite accurate, is rather below than above the truth.

While the nerve cells or neurones are strikingly uniform in general external morphology, still microscopic examination shows that the length, mode of branching and size of the cell processes, together with the relation in which they stand to

the cell body, affords ample opportunity for the production of varied appearances, and in the different groups of nerve cells (for as might be easily imagined even among specialized workers belonging to one colony, where the colony contains thousands of millions of individuals, there is further specialization, division of labor, and accordingly formation of multiple subgroups), one meets with structural peculiarities which permit a skilled histologist to decide, even from the external form alone, as to the particular group to which a given neurone belongs. Thus, in the diagram, no difficulty is encountered in distinguishing a pyramidal cell of the cerebral cortex, from a Purkinje cell in the cerebellum, a motor cell from the ventral horn of the spinal cord, or a cell from a spinal ganglion.

The researches of the cytologists, in addition to supplying us with data concerning the form of the outside of the neurones and their processes, have added a wealth of detail concerning the internal structure. Each neurone, like every other cell individual of the same order, contains a nucleus with one or more nucleoli embedded in the protoplasm. In addition, in many nerve cells the existence of centrosome and archiplasm has been demonstrated, and it is not impossible that all nerve cells contain these peculiar differentiated structures. In nearly all nerve cells, after treating with fixing reagents, the protoplasm of the dendrites and of the perikaryon can be seen to be made up of at least two substances (aside from the so-called pigment met with in many nerve cells); (1) a substance consisting of very minute granules, arranged in masses which have the form of dots, rods, spindles, wedges or cones, the so-called Nissl bodies, tigroid masses, or chromophile corpuscles; these show an especial affinity for certain dyes, contain iron and phosphorus, and are soluble in alkalies, and (2) a ground substance, in the fresh condition, and by some methods of preparation almost homogeneous in appearance, stainable by an entirely different set of dyes, resistant to weak alkalies, but digestible in artificial gastric juice.

There is a good deal of evidence that the first substance, that corresponding to the Nissl bodies or tigroid, is present in the living cell in solution, that it is allied in composition to the nucleo-albumins, and that it represents in large part the food supply of the nerve cell. The fact that it is present in about the same quantity and distribution in nerve cells of the same group, and that it varies considerably in quantity and distribution in nerve cells of different groups, when studied by a particular method, makes it of high importance for the anatomy

and pathology of the nerve cell. This substance is present in the perikaryon and dendrites, but no ascertainable amounts of it exist in the axone or in the portion of the perikaryon directly continuous with the axone, the so-called axone hillock. It must be extremely labile, for the quantity and distribution can be speedily and remarkably altered by insults of various kinds, mechanical, chemical or thermal, applied to any part of the neurone. It may even be made to entirely disappear from the nerve cell for a while, to return again some time after the cause of the disturbance has been removed. No direct relation, however, between the symptoms manifested by the animal as a result of the insult and the change in this tigroid substance can at present be made out, for on the one hand the symptoms may be out of all proportion to the changes recognizable in this substance, and on the other the alterations in the substance may continue for a relatively long period after the unusual symptoms have disappeared.

The structure of the second substance, that which we have spoken of as the ground substance of the nerve cell protoplasm and sometimes referred to as the "unstainable substance of Nissl," is as obscure as is that of protoplasm in general. In the perfectly fresh condition it seems to be under the highest oil immersion lenses quite homogeneous, but that it is not entirely homogeneous is rendered likely by a consideration of the effects of certain reagents upon it. Thus it is easily vacuolized, and the vacuoles when formed, though varying in size with the different reagents which can be employed, tend to recur in the same variety of nerve-cell constantly in the same arrangement. Thus the character of the vacuolization differs in the dendrites from that in the main protoplasmic mass, and the vacuolization in both dendrites and perikaryon is again very different from that of the axone. In such vacuolized preparations, certain particles, sometimes lying in the vacuoles, more often lying in the protoplasmic walls intervening between the vacuoles, can be stained by suitable dyes. These are the so-called neurosomes, and they also differ much in number and arrangement in the various parts of the neurone, being most abundant apparently in the protoplasm of the terminal ramifications of the axones and collaterals.

By special methods of fixing and staining, fibrils have been observed from time to time inside the ground substance; some of these are doubtless identical with the walls of the vacuoles seen in other preparations. Recently, however, very definite fibrillary appearances have been demonstrated inside the neu-

rones of both invertebrate and vertebrate animals, and it would appear that these represent special morphological entities differentiated from the rest of the nerve cell protoplasm. In invertebrates coarser fibril-like structures running through the axones and dendrites of neurones are described as breaking up in the perikaryon into a relatively large number of simpler fibrils, which anastomosing freely with one another unite to form intricate intracellular networks. In human nerve cells, by a somewhat different method, similar fibrils can be demonstrated in the processes, and in the perikaryon, but, it is said, without the formation of anastomoses or networks. Single fibrils can be traced through the perikaryon from a dendrite to an axone or from one dendrite to another dendrite of the same neurone; it is even stated that a fibril running for some distance toward the perikaryon in one branch of a dendrite, may before reaching the perikaryon turn back into another branch of the same dendrite and run in the opposite direction.

With regard to the ground substance of the nerve cell protoplasm, morphological knowledge is far in advance of explanations of physiological significance. Certain it is that this ground substance is of the highest importance for the nerve cell functions—certainly of infinitely greater importance than the stainable substance of Nissl. For while the latter can be markedly disintegrated or even obliterated from the nerve cell structure, and yet complete recovery follow, any pronounced general alteration in the ground substance is inevitably followed by complete degeneration and death of the whole neurone. Certain portions of the ground substance may, it is true, be destroyed without necessarily causing the death of the whole nerve cell; indeed, disintegration of all the ground substance forming that portion of an axone distal to the lesion when an axone be cut need cause no permanent injury to the neurone; the portion of the neurone which remains may regenerate the part removed.

We feel tolerably certain from recent experience, that the ground substance of the nerve cell protoplasm is the portion of the neurone more especially concerned in the nerve functions proper, but whether it acts as a whole, or whether, as would seem more likely, the structures differentiable in it, such as the neurosomes and fibrils, are of different physiological significance than the more homogeneous parts, the data at our disposal do not permit us to decide. Some investigators have been tempted, very naturally, I think, to assume that the fibril-like structures in the ground substances represent the essential con-

ducting substance, but, however plausible, this is not yet satisfactorily proven, and even if such structures were shown to be particularly suited for conduction, a similar function for other parts of the nerve cell protoplasm would be by no means excluded. In passing it may not be superfluous to remark that, lucky as we should be to establish clearly the element or elements actually concerned in *conduction* in the nervous system, such establishment would refer to only one feature of neuronal function, and the capacities other than those of mere conduction would have to be subsequently considered. Time will not permit me to enter into a discussion of the morphological and physiological facts which have been accumulated with regard to the nucleus; it will be sufficient to say that they are probably just as important, if not more important, than those of the protoplasm, and that as yet our knowledge of them is even less complete.

A word as to intercellular or interneuronal substances inside the central nervous system. I have already spoken of the periaxonal myelin, and have referred to the reticular investment of the perikaryon and dendrites. That the blood capillaries give off a nutrient fluid which bathes the nerve cells there can be no doubt; that the neurones throw off excrementitious substances into the lymph is just as certain. Whether in addition to this lymph, and the products of the neuroglia and ependyma, there are besides the perineuronal myelin and reticular investment any formed intercellular substances derived from the neurones, we do not know. The majority of investigators at present are opposed to the assumption. For the neuropilum of invertebrates, however, it is asserted that fibrils similar to the intraneuronal fibrils exist entirely free, and a well-known German neurologist has recently made a strong plea in favor of the view that in the grey matter of the central nervous system of vertebrates, and especially of man, similar extraneuronal fibrils exist in large numbers, and are accountable for the peculiar stamp which the grey matter bears. From what we know of other tissues in the body, and from what we have learned of the fibril-building power of neuroglia cells, the existence of such intercellular substances in the nervous tissue is not incomprehensible, nor would the demonstration of their presence be a matter of surprise. Thus far, however, this demonstration is lacking and we need scarcely worry ourselves concerning the possible function of such hypothetical substances before their existence has been proved. That the bringing of such proof could fundamentally alter our general conception of the struc-

ture of the nervous tissues or of the body as a whole, I find difficult to conceive, for as every histologist who has worked with the tails of rats, the ligamentum nuchae of the ox, a piece of hyaline cartilage, or a mass of bone, knows, the occurrence of an intercellular substance is no strange phenomenon and exercises no restraining influence on the formation of the idea that the body essentially consists of a mass of cells or individuals of a lower order, united and co-ordinated into a single individual of a higher order—the whole organism.

It would take too long to review even briefly the main facts concerning glia cells, ependyma cells and glia fibres. An epitome of the changes which the nerve cells undergo in the body of the embryo and after birth before they have assumed the form met with in the adult must also be omitted. That in early stages the nerve cells are devoid of processes, are motile, and multiply by karyokinesis are now well-known facts. Independent of one another and wandering from their birth-places, the neurones gradually develop their wonderful processes, first the axones, later the dendrites and finally come to occupy, some of them sooner, others later, the localities in which they are destined to spend the remainder of their lives.

So much for the modern conception of the histological units in the nerve tissues. The neurologist is in possession, however, in addition to the special knowledge which concerns these units or individuals, of much valuable information bearing upon the inter-relations of the units, the way in which they are grouped, the possibilities of reciprocal influence not only among members of a single group, but among the groups themselves, in short, the architecture of the central and peripheral nervous organs. He sees how that among an enormous number of individuals, of the order of body cells in the process of physiological integration which leads in normal animals to a united functioning as a higher and more complete vital unit, a series of units morphologically and physiologically intermediate have arisen. Neuronal mechanisms are combined to make neurone-group mechanisms, neurone-group mechanisms are combined in turn to give rise to mechanisms of still higher orders, until finally the whole nervous system is included. The latter, constantly acting upon the rest of the body and the environment, and in turn being influenced continuously by the rest of the body and its environment, we stand face to face with the organism as personality.

It would take many lectures of the time allotted to this to deal with the features of this organization with which we are already

familiar. For we should have to consider the gradual transition in the organismal series from unicellular animals, in which the response to a stimulus has to be made by the same cell which receives it, through a long chain of ever increasing complexity in which there is dissociation of the primary stimulus from the ultimate response and the intercalation between the two of one, two, one hundred or perhaps many thousands of neural activities. In multicellular organisms with the increase of functional complexity there is corresponding increase in the number of special laborers, and progressive dissociation of the function with distribution of special tasks among these laborers. A brain appears, a general movement center in connection with one or more organs of special sense (Steiner). In the highest of animals, consisting as he does of a large number of partially fused segments, each segment fitted out with a relatively independent sensori-motor apparatus formed architecturally of a set of receptive neurones closely related to another set of discharging neurones, the individual segments in turn being manifoldly united by commissural and association neurones with one another and with higher groups of neurones, we meet with the acme of dissociation of neural function combined with the highest known order of complex unitary neural capacity.

We are learning to recognize the anatomical mechanisms which account for the fact that the application of sensory stimuli to the skin or tissues belonging to a primitive segment, while primarily influencing by way of neural channels, the musculature or the secreting glands of the same primitive segment, may secondarily excite similar tissues of adjacent or even widely removed segments; for the fact that the same sensory stimulus which sets free reflexes can also play a part in the origin of an instinctive reaction or even enter as an important component into the genesis of a voluntary act; for the fact that groups of elementary sensations resulting from stimuli originating in the body itself or in the external world can be united into physiological units of higher orders, into feelings or emotions, into more clean-cut perceptions and even into abstract ideas and conceptions; and also for the fact that subconscious afferent impulses, strong feelings and mature reasoning can all excite motor discharges, in the one case suddenly as an immediate and necessary response to the stimulus applied, in the second instance less promptly perhaps and modified by intercurrent factors, and in the last event more slowly with the manifestation of all the characteristics of a deliberate choice.

I say we are learning to understand these anatomical mechanisms, for I do not mistake the beginning for the end. What we know is but the threshold to that more complete knowledge, the treasures of which contemporary neurologists are beginning to catch a glimpse. Fortunately for medicine and for mankind this threshold is that of an "open door," entrance to which is barred by no political constitution or jealous state enactment; portions of the wealth beyond are available to any one who possesses natural aptitude, and who, approaching it with reverence, interest and industry, is willing to make his aptitude of value by submitting for a time to that rigorous training by which alone it is possible to acquire the necessary technical skill.

This brings me naturally to the discussion of the methods of neurological investigation that have led to that knowledge of the nervous system which we already possess, and that together with new methods, sure to be discovered as we continue to work conscientiously with the old ones, are destined to expand our views, to open up new neurological vistas and to illuminate those now seen only in the dawn.

On examination it is, perhaps, not surprising to find that these methods can be divided into two groups which stand in intimate relation to the two aspects of function which we have learned to distinguish in our study of the nervous system. We have seen in this system how through the subdivision of the labor among a large number of individuals there has arisen a marked dissociation of functions, and how through fusions of the activities of dissociation-mechanisms the higher and higher unitary physiological activities are to be accounted for. In the study of the nervous system, also, methods of dissociation or analysis have to be combined with methods of integration or synthesis in order that the most satisfactory results in either morphology or physiology can be reached. It is a universal experience that in the progress of acquiring knowledge analytical methods precede the synthetical. There must be differentiation before integration. Now, while a whole series of analytical methods have been in use for a long time and have of late been wonderfully refined and rendered extremely delicate, it is striking that there are but few synthetical methods, and those that have been employed have been relatively crude, the better methods having been used only by a limited number of investigators.

I shall not be so inconsiderate as to detain you by describing, even briefly, the technique of the various methods which have

been and are still helpful, but shall be content with recalling to mind the special advantages of the principal ones and, perhaps, the names of the investigators deservedly associated with some of them. What I shall say in this connection will bear solely upon morphological studies.

The earliest workers occupied themselves mainly with describing the gross form relations of the central and peripheral nervous systems as revealed on simple exposure by removal of the bony and membranous coverings or by cutting into the organs. The shape of the principal masses and cavities, the existence of white and grey substance, the distinction of the cerebrospinal and sympathetic nervous systems and certain gross pathological alterations were early known and described. Coincident with the increased study of human material and greater skill in the use of the scalpel the descriptions become gradually more accurate until in the records left behind them by such men as Sylvius, Vesalius, Monro, Sir Charles Bell, Lockhart Clarke, Reil, Rolando, Burdach and Stilling, we cannot but marvel at the accuracy of observation and the faithfulness of portrayal which they manifested.

The introduction of hardening fluids facilitated the study of gross material and by preserving the tissue from decomposition permitted the prolongation of the examination of a single specimen indefinitely. Thick slices of the hardened tissue yielded in many respects more satisfactory information than that derivable from slices of the fresh soft organs. Alcohol hardening permitted of successful manipulation with fingers and forceps and the newer conceptions gained with the aid of the *Abfaserungsmethode* were at the time justly lauded. In this connection the work of Burdach, Reil, Foville, Stilling and Meynert deserve especial mention.

Late in the last century and early in the present the method of isolation of parts was pushed further, especially when the microscope came into more general use and methods of teasing with needles and of loosening the parts from one another by means of fluids which soften or dissolve out certain of the substances which ordinarily prevent dissociation were introduced, and the knowlege of the nervous organs became within a relatively short time enriched to an unprecedented degree. The details made out concerning isolated nerve cells and their processes and separated single nerve fibres and their coverings by these relatively simple manipulations were truly remarkable. The histologists of the time attained to a degree of skill in this field which would give the blush to the modern histologist

did he attempt to imitate them. In this connection Wagner, Deiters, Max Schultze and v. Kölliker, are the names one thinks of. The student of neurology to-day will do well if he do not despise or neglect a form of examination which affords pictures of the parts obtainable by no other means.

As early as 1824, Rolando had cut sections of the nervous system and examined them under the microscope. It was in 1842, however, that Stilling, having cut a frozen section of the spinal cord and recognized the ease of the study of relations inside it, exclaimed "eureka" and caught a gimpse of the great possibilities of the application of the method of the study of *serial* sections. Since then microtomes have been invented and wonderfully improved, satisfactory methods of embedding have been devised, and now it is possible to cut the whole brain of an adult man into faultless serial sections in any one of the three dimensions of space without loss of a single section. Recently Flatau has shown that it is possible also to divide the whole spinal cord into longitudinal serial sections. By means of absorption, embedding, serial sections of one or a few nerve cells can be obtained as thin as one micron or even less.

Next in importance to mechanical subdivision of the nervous system into its morphological elements and into extremely thin slices, was the invention of the method of differentiation by means of the application of coloring matters of various sorts. The carmine method of Gerlach in connection with bichromate hardening of the tissues not only differentiated the nuclei of the nerve cells from the protoplasm in which they were contained, but by showing a special affinity for the axis cylinders of the nerve fibres rendered them easily distinguishable in sections from investing sheaths and from neuroglia elements The impregnation with chloride of gold also revealed minute nerve fibrils and processes of nerve cells which must have appeared most remarkable to those who, studying tissues, prepared them in this way for the first time.

Of even greater importance was the introduction of Weigert's stain for myelin sheaths which made it possible to follow bands of medullated fibres or even single medullated fibres for long distances in the central nervous system and in the peripheral nervous system. The method is valuable not alone for the study of the adult nervous system of man and animals in health, but because in diseased conditions it also gives information of the very highest import, since in areas in which the medullated nerve fibres have undergone degeneration from any cause and have been absorbed, the absence of bundles of myelin sheaths

from positions in which they normally exist is demonstrated in a superb manner. And while the extremely delicate method of Marchi will indicate the existence of degenerated nerve fibres at a much earlier period than that corresponding to the total absorption of these fibres, and is accordingly a boon to the experimental investigator, it can never entirely replace Weigert's method for the study of degenerations. Indeed, in human pathological anatomy the two methods supplement one another most conveniently.

As a special application of Weigert's myelin sheath stain may be mentioned Flechsig's studies of the developing nervous system. The discovery of the fact that the bundles of medullated nerve fibres which exist in the adult nervous system do not all receive their myelin sheaths at the same time, but get them rather at successive intervals corresponding more or less accurately in serial appearance to the successive manifestation of more and more complex functional activities, gave the clue to the embryological analysis of the medullated tracts, which having thrown and still throwing so much light upon the architectural characters of the spinal cord and brain, will always be associated with Flechsig's name.

The latest results of this application of this method has resulted in Flechsig's hands in the better localization of the primary sensory motor areas in the cerebral cortex, in the demonstration of the fact that the projection fibres connecting these various areas with lower parts of the central nervous system are medullated at different periods and in the discovery of the existence and topographical distribution of the secondary centers of a higher and fundamentally different significance—the so-called association centers of the cerebral cortex.

Through improvements in the compound microscope, especially by devices for increasing the illumination and for the elimination in large part of the spherical and chromatic aberration, it has been possible to obtain a clear definition of microscopic objects, even when magnified 1,000 or 2,000 diameters. The extension of the powers of the human retina thus made possible, together with the advances in staining, clearing and mounting, have revolutionized the science of histology and microscopic anatomy, and the old-time six weeks' course given in these subjects has been replaced by one of as many months. Cytology in general has made enormous strides, and with it cytology in particular, although curiously enough the nervous system, owing to the peculiar character of its cellular elements, did not reap the benefits quite so soon as did

the other organs of the body. But when once results began to be attained in the nervous system by these methods or by particular modifications of them suited to the special structure of the nervous organs, they came with a rush, and during the past two decades the world has been flooded with books and original articles in morphological journals dealing with the results of research into the histology and architecture of the nervous system. To Golgi, of Padua, belongs the credit of devising a form of metallic impregnation which better than any other procedure outlines the external form of the nerve cell and its processes, especially in embryonic tissues. Utilized by many students in many countries, this method has taught us how complicated the various processes of the nerve cell really are; it has shown us the external morphological differences between dendrites and axones, the varying appearance of these structures in the same part and in different parts of the central nervous system, and has given us an insight into the various inter-relations which exist among the cellular units of which the system is made up. Very recently, by slight modifications of the method, Golgi has shown that it can be utilized to demonstrate not only the reticular investment of the perikaryon and dendrite, but also certain curious network-like appearances inside the nerve cell protoplasm. The objection, therefore, that Golgi's method affords no information with regard to the interior of the neurones can no longer with justice be urged.

The method of vital staining with methylene blue or thionin, invented by Ehrlich, not only confirmed in large part the findings arrived at with Golgi's method, but also extended them. A special advantage of Ehrlich's vital staining lies in the fact that with it the axones of medullated fibres can be stained; whereas, with Golgi's method the impregnation of an axone usually ceases as soon as the myelin sheath is reached. By means of the method of fixation which we owe to Bethe, the transitory pictures obtainable by the vital staining may be caught at the acme of development and rendered permanent.

Among the host of cytological methods which are suitable for the investigation of the interior of the nerve cell that introduced by Nissl has been extensively followed up. It consists of alcohol fixation, sectioning without embedding, staining with the methylene blue and soap mixture, differentiating with aniline oil and alcohol and mounting in benzine colophonium. It is especially valuable for the examination of the neurones under normal and pathological conditions with respect to the amount of the stainable substance of Nissl present in them

and its distribution in the cytoplasm. Other similar methods, such as thionin staining, toluidin blue staining or double staining with methylene blue and erythrosin, offer special advantages for certain purposes.

To demonstrate the neurosomes, fixation in a neutral solution and staining with iron haematoxylin (Held) serves admirably. Fibrillary appearances are discoverable in tissues fixed in chrom-osmo-acetic acid and stained in saffranin (Fleming). They are exquisitely stainable in invertebrate tissues by a sublimate gold method and by a haematëin stain (Apáthy); while in vertebrate tissues they are most easily demonstrable in cells which have been treated first with ammonia, afterwards with hydrochloric acid, then with molybdic acid and finally with toluidin blue (Bethe). The action of alkalies, acids and digestive agents of various kinds should also be mentioned

Concerning the synthetic methods there is but little to say, inasmuch as the sole procedure which has been employed by the majority of neurological investigators is the mental fusion of the pictures obtained by isolation and sectioning into more or less vague ideas of solidity. Actual reconstruction in tangible form of the solid bodies in the nerve tissues from a faultless series of sections has been carried out only by a limited number of workers.

This method originated with the embryologists and grew out of the desire felt by investigators to reproduce exactly in three dimensions the magnified details of external and internal form as studied in microscopic sections. If an embryo be cut into serial sections, and section after section be studied, the exact relations in the individual sections can be easily made out. But even anatomists endowed most liberally with what may be termed the spatial sense find difficulty in uniting a long series of sections through several bodies as seen through the microscope into an integrated, accurate conception of the solid bodies thus magnified. My experience teaches me that a relatively large number of students are almost absolutely devoid of this power of integration, or as it is sometimes expressed, of thinking in three dimensions when studying a series of sections. For the purpose of coming to more accurate conclusions himself, and especially with the object of making certain form conceptions clear to students, Wilhelm His, of Leipzig, many years ago introduced his method of graphic reconstruction from serial sections. His procedure is so generally known that I need not take the time to describe it in full. He used, it will be recalled, paper ruled at distances cor-

responding to the thickness of the sections multiplied by the magnification employed. The outline drawing of the whole object over these lines thus permitted the introduction on the parallel lines of the paper the limits of any desired object in the various sections. In this way extremely valuable flat projections of the various internal organs and tissues could be obtained, and the method is a favorite one at present with many embryologists.

From a series of projections of the organs as viewed from different aspects it is possible for an artist to model them in clay or wax. Thus there arose through the combined activities of His and Ziegler the exquisite models illustrating various stages of development of the embryo chick which are nowadays a feature of so many anatomical museums.

Not all investigators, however, are gifted with the mathematical knowledge and artistic talent necessary for the successful application of the method. Somewhat later reconstruction with the help of wax plates, permitting the making of wax models directly, from the specimens, was introduced by Born. In the 22 years which have elapsed since he first employed the method many improvements have been made, so that a number of technical difficulties with which he had to contend can be avoided. It is this method of reconstruction modified and improved which Dr. Mall has used so successfully in the study of the anatomy of his series of human embryos. It is also this method which Miss Sabin, with the aid and counsel of Dr. Mall, has employed in the construction of the model of the medulla oblongata, pons and mid-brain which I here show you.

The prerequisites to the work are (1) the possession of faultless serial sections of the objects to be studied stained in a suitable manner; (2) an intelligent idea of the general relations and significance of the contents of the sections as seen through the microscope; (3) suitable mechanism for the production on paper or directly on the wax plates of the magnified picture of the section (camera lucida or Zeiss projection apparatus); (4) wax plates of proper dimensions and consistence; (5) the guidance of an experienced workman; (6) patience, industry, enthusiasm and a certain amount of spatial sense and mechanical skill.

We are fortunate enough to possess in the anatomical laboratory at Baltimore several sets of serial sections cut in various directions through the brain stem and cerebral hemispheres of human fœtuses and babies of different ages illustrating accordingly different stages of development.

The early form relations of the human nervous system have been worked out by His, and his results are embodied in his well known series of models. Last year Mann, of Edinburgh, presented at the anatomical society reconstructions of single nerve cells. Thus far, however, no one, to my knowledge, has published the results of reconstruction of the medullated tracts in the human nervous system. It has occurred to us that the analysis of tracts rendered possible by the embryological method of Flechsig offers a most suitable field for the application of the reconstruction method. A number of students may, we believe, conduct such investigation satisfactorily, and without interference with their regular medical studies. The task of making such reconstructions was accordingly assigned and a number of models are now in progress. The first fruits of the work are represented by this model upon which Miss Sabin has been engaged in the time she could spare from her regular studies since one year ago last March.

The portion of the brain represented by the model is that of a human fœtus near full term. It was cut into horizontal serial sections and stained by the method of Weigert-Pal by Dr. John Hewetson in the anatomical laboratory of the University of Leipzig. Circumstances preventing Dr. Hewetson from continuing his work with the specimens, he was kind enough to place them at the disposal of instructors and students at Baltimore.

After some preliminary study of a series of transverse sections through the medulla, Miss Sabin made a more careful study of the series of horizontal sections until she was sufficiently well oriented with regard to the principal medullated tracts and grey masses to proceed with the actual work on the model. Every other section, by means of the Zeiss apparatus and electric illumination, was projected, magnified 14½ diameters in a dark room upon a sheet of white paper, and the outlines of the tracts and nuclei were drawn in accurately with lead pencil. This outline drawing was subsequently made entirely accurate with regard to certain details by control studies with higher powers of the microscope. After all the drawings had been made and corrected each one was accurately transferred by means of carbon paper to wax plates, numbered to correspond, each wax plate, of course, representing in thickness 29 times the thickness of the individual sections. To facilitate subsequent manipulations the areas on the wax plates were painted in various colors.

The wax plate sections once completed, it was necessary to cut out the various areas and to begin piling the sections of the

different tracts and nuclei upon one another so as to reproduce the exact form magnified $14\frac{1}{2}$ times in the three dimensions. Here the investigator meets with his greatest difficulty, and it is just at this juncture that natural mechanical skill, as well as experience, count for much. In order to pile the pieces correctly the worker is helped enormously by (1) a knowledge of the external form of the whole object before it was cut into serial sections, and (2) a knowledge of one or more localizable perpendiculars or curves which can be used as a guide. There need be no trouble about the external form if an accurate drawing from three aspects or photographs of the object have been made to scale before the sections are cut. Unfortunately in the present instance no such drawing or photograph was obtained, and Miss Sabin had to resort to a method discovered independently by Selenka and Mall, which obviates the difficulty. Several brain stems of fœtuses of the same age were studied in the gross with particular reference to the external form. The drawings of the sections were then cut out (whole) of the wax plates and piled repeatedly until the type form as learned from the study of other specimens was approximated as nearly as possible. Then the waste of the wax plates, that is, the boundaries of the holes after the drawings of the sections were cut out, were piled up in an exactly similar manner. A cast of the holes was then made with plaster of paris, the wax picked off, and the external form permanently preserved as a guide.

As to the establishment of perpendiculars and curves, the middle line of the sections of the symmetrical nervous system serves admirably in the one dimension; for the other two dimensions the curves of the external form were followed, helped out of course by the known distances of the individual structures from one another in the different sections. The stratum interolivare lemnisci and lemniscus medialis were first modelled and the other structures built up about these.

The various ingenious contrivances which had to be invented to work out successfully many of the details of the structure may be passed over at this time without mention. They will doubtless be described by Miss Sabin in full in her publication. After the various parts had been reconstructed and the edges smoothed with a hot iron the medullated bands of fibres were painted white, the motor nuclei blue, the nuclei terminales of the sensory nerves red, and other grey masses yellow.

At first glance the gross relations represented by the model are clear—the upper extremity of the spinal cord, the medulla oblongata, the pons and the mid-brain. The remarkable curves

made by the central cavity (1) at the junction of the central canal of the cord with the fourth ventricle and (2) in the region of the aqueductus cerebri are illustrated. The medullated tracts of the cord can be followed upward into the rhombencephalon. The division of the nervus acusticus into its two components, and their relations to the corpus restiforme, and their nuclei terminales are observable. It is seen that the nucleus nervi cochleae ventralis forms a continuous mass with the nucleus nervi cochleae dorsalis lying lateral from the corpus restiforme. The situation of the striae medullares is indicated. At the isthmus the nervus trochlearis of one side undergoes decussation with its fellow of the opposite side.

On removal of the nervus acusticus and the corpus restiforme, the course of the ascending and descending limbs of bifurcation of the fibres of the nervus vestibuli can be studied as well as the relations of these to the various terminal vestibular nuclei—the medial, the superior, the lateral nucleus, and that of the descending root.

The modelling of the nervus trigeminus with its motor nuclei of origin and sensory nuclei of termination has been particularly instructive. The course of the tractus spinalis nervi trigemini, the division into a larger lateral and a smaller medial portion, the relations of these bundles to the substantia gelatinosa, the descending mesencephalic root, the minor motor nuclei and the principal motor nucleus and the relations of the motor nuclei to the portio minor of the peripheral nerve—all are evident. The fibres of the nervus glossopharyngeus and of the nervus vagus now come into view, and it is seen how large a mass of the glossopharyngeal fibres go to form the tractus solitarius. The relations of the motor fibres to the nucleus ambiguus and of the sensory fibres to the nucleus alae cinereae are demonstrated.

These two large masses of grey matter painted yellow, fitting so accurately into these irregular cavities in the white matter which represents the medullary continuation of the dorsal funiculi of the spinal cord, are the nucleus funiculi gracilis and the nucleus funiculi cuneati respectively. The difference in the distribution of internal arcuate fibres derived from the two nuclei is obvious.

Removing the last mentioned structures the funiculus lateralis, and the bundle of fibres going into it from Deiters' nucleus can be better examined. The motor nuclei of the medulla are now well exposed, and the division into a lateral group and a medial group is seen. The nucleus ambiguus and

the nucleus nervi facialis are evidently members of the lateral group, while this long curved nucleus nervi hypoglossi and the nearly spherical nucleus nervi abducentis are more medially placed. The old bugbear of the raw student in neurology—the course of the nervus facialis inside the medulla—has lost its terrors, for here pars prima, genu, and pars secunda are all seen at once, the excursion around the sixth nucleus is evident, and the final plunge through the corpus trapezoideum to the outside can be readily followed. Higher up the motor nuclei of the nervus trigeminus, the nervus trochlearis, and the nervus oculomotorius are seen. The inclined plane formed by these upper eye muscle nuclei is rarely understood from the study of transverse sections alone, although in sagittal sections of course the inclination is obvious.

Let me call your attention to the plastic representation of the lateral lemniscus and the medial lemniscus. The relations of the lateral lemniscus to the corpus trapezoideum, to the superior olivary complex, and to this long drawn out nucleus lemnisci lateralis which lies in a trench on its lateral surface, as well as the intimate connection of a large part of the bundle with the colliculus inferior of the lamina quadrigemina, are prominent features of the model. No less instructive is the illustration of the origin, course and distribution of the fibres of the medial lemniscus or fillet. Starting below as a vertical mass of fibres—the stratum interolivare lemnisci—formed in large part of internal arcuate fibres which have crossed the raphe from the opposite side of the medulla, it is continuous dorsally in the first part of its course with the fasciculus longitudinalis medialis or so-called posterior longitudinal bundle. Higher up the two bundles are separated by masses of grey matter and from the corpus trapezoideum on, the medial lemniscus, now much increased in volume, alters its position and direction, spreading out as you see into this large curved fan-shaped mass.

Miss Sabin's model of the brachium conjunctivum supports very conclusively the view that the ventral part of the decussation of the brachia of the two sides represents a vestibular commissure. The pocket between the ventral and dorsal portions of the decussations is here visible, and is very satisfactory to note that the portion of the brachium conjunctivum on each side corresponding to the ventral decussation is related directly with the antero ventral extremity of the nucleus nervi vestibuli superior or Bechterew's nucleus. The results which concern the fasciculus longitudinalis medialis, the formatio reticularis alba et grisea, the decussationes tegmento-

orum, the nucleus ruber and the bundles of white fibres near it, the fasciculus retroflexus of Meynert, and the substantia nigra are of interest, but to fully appreciate them or indeed any part of the model it is necessary to study the serial sections along with the reconstructed parts. It is in this way alone that the value of blending the areas met with in the individual sections into the solid wax bodies can be fully appreciated, and a real mental coalition effected.

One can hardly fail, I think, to be interested in the appearance of the nucleus olivaris inferior, here for the first time, I believe, accurately reproduced in three dimensions. To me it is one of the most instructive parts of Miss Sabin's work. Every one who has studied the olive in sections knows that the grey matter is repeatedly depressed and elevated on the surface, and each of us probably has formed some vague idea of the wrinkled shell corresponding to the whole structure. But who would have guessed that the olive presents the remarkable appearance we see here! It is obvious on examination that the lateral surface is divided by deep fissures into lobes, and that each of these lobes is further subdivided by shallower sulci into gyri. That these sulci and gyri are no accident, but tolerably constant features, is clear from the reconstructed olive of the opposite side, which is almost the exact counterpart of its fellow. Since the gyri and sulci are as definite and characteristic as those of the cerebral cortex, Miss Sabin will, I have no doubt, name them for convenience of description. If the medical student of the future had to learn by rote the new lists of names which such studies are constantly thrusting upon us, he would indeed need to be commiserated, but fortunately instructors and examiners are becoming more sensible than their predecessors in what they demand of their students.

This method of wax reconstruction, then, represents the most accurate of the integrative methods at present at our command. In the solution of morphological problems connected with organs the most complex in architectural arrangement in existence on this planet it is capable, I believe, of wide application. That it will, sooner or later, have served its purpose and be replaced by more delicate and accurate integrative methods yet to be discovered, there can be but little doubt, for while on the one hand those who are familiar only with the mental arithmetic reconstruction in general employed, are much impressed when they first become acquainted with the wax plate method, with the beauty and accuracy of the spatial concepts attainable through it; on the other hand, those who know it best and are

familiar with the history of technical procedures in the past, are conscious of its crudeness and aware of its limitations, and they are prepared for, and will welcome the time when we shall be presented with three dimension reproductions of the nervous organs as much superior to these wax plate models as the latter are to the less accurate, but at the time of their production extremely valuable schematic models of an Aeby or a Cazeaux.

Before closing this lecture, which I fear has already made too great claims upon the graciousness and patience of some of you, I must beg your indulgence still further for a moment in order to refer briefly to the importance of more systematic neurological instruction in our medical schools, the value of combining such instruction with neurological investigation, the necessity, in order to accomplish this end, of the development of better teachers and more perfect laboratories and laboratory organization, and finally of the benefits derivable from a better understanding of one another's aims among laboratory investigators and clinicians, and from such co-operation among these as may, while in no wise interfering with individual liberty, permit of the direction of their specialized activities along the lines of a more or less co-ordinated plan.

It has for several years past seemed to me a striking anomaly that so little provision has been made, even in medical schools generally recognized for their excellences, for the study of the structure and function of the human and animal nervous system, especially since everyone prepared to think accurately and who has given the subject thought, readily admits that it is precisely by virtue of his neural pre-eminence, rather than by marked special advantages in other parts of his body, that man ranks first among the animals. The difference, too, between individual men lies in large part in differences in nervous organization, and, indeed, it is owing largely to our knowledge of differences in brain morphology and brain capacity that we can, without fear of successful contradiction, designate the statement, "All men are born free and equal," one of the greatest fallacies which has ever moved large bodies of men into action. When we remember this and recall the large proportion of ailments which have a neural or psychic element in them, is it not surprising, to use as mild a word as I dare, that a more or less extended knowledge of the anatomy and physiology of the nervous system has not been regarded as of essential importance in the training of the medical man? It is not long since when even distinguished professors of medicine in our best medical colleges were brave enough to admit—indeed, seemed delighted to

jocularly confess—that they "never could understand the fillet." But while at that time knowledge was so limited and the means of acquiring the little possessed were so inadequate that such a confession was one of which he who made it need not necessarily be ashamed, that period is now happily past and we have entered on an era in which neurological facts tolerably accessible and of extreme practical usefulness are by no means few in number. It is owing to our ignorance of the anatomy and physiology and pathology of the nervous system that we are unable as yet to manage as successfully as we would that host of so-called functional nervous disorders which unhappily are becoming so prevalent among us, and it is in large part due to this ignorance that the flora of "the Garden of Cagliostro" is so rank and luxuriant. Not until medical men understand psychology and learn how to recognize and cope with the psychic factors of disease and ignorance need we hope to prevent the access to "Gloria mundi" of some disciple of the Prince of Quacks.

A study of the early records which have come down to us teaches us that in ancient times the healing of the body was entrusted to the priests, who thus ministered to the physical as well as to the spiritual needs of their people. Since then the science and art of medicine have become separated from the priesthood. But is it impossible that at some time in the not very distant future, when through the fusion of converging lines of research psychology has come to be recognized in its normal relations as a department of physiology, psychiatry as a department of pathology, a re-distribution of labor should take place and the functions of physician of the body and physician of the soul come again to be united in a single individual?

Two great difficulties at present obstruct progress. (1) The lack of trained individuals to serve as teachers and to conduct research, and (2) notwithstanding the remarkable multiplication of so-called laboratories, the lack of appreciation of the importance of suitable laboratory organization. Any one living in one of the large centres of medical education, in touch with the leaders of medical thought in such places and conversant with the extraordinary demand for trained men to undertake responsible laboratory and clinical positions, when he sees the difficulty of filling such positions, cannot fail to lament the gross errors of the system of education responsible for this condition. In a country full of young men with great natural aptitude and unprecedented adaptability, it is a pity to

have to confess a dearth of men with real skill. This is not the fault of the men, but the lack of opportunity for adequate training. A wave of educational reform in medicine and in the natural sciences is sweeping over this country at present. The faults of the older régime are being recognized and the prospect for the future, I am glad to say, is bright.

Medical faculties have been too prone to imagine that the construction of large lecture halls and magnificent laboratory buildings will suffice for the development of a productive department and the institution of adequate instruction, but too often they are disappointed in the results. A shrewder foresight and a wider wisdom puts its money into *men*, the other necessaries follow of their own accord.

That much of the best talent and capable brain is diverted from scientific channels in a country where for comfortable existence considerable sums of money are necessary, is easily understandable when one remembers how meagre the pittance so often accorded to the holder of a scientific chair and how much greater the same talent and the same brain capacity can command in a different market.

But given a good laboratory and given a good man, the conditions for successful instruction and investigation are by no means fully satisfied. An institution nowadays can no longer hope to succeed by taking a scientist into a brick box and saying to him, "Robinson Crusoe, here is your island." The director of the laboratory must be accompanied by trained assistants, and it is desirable that these assistants, though, perhaps on the whole, equally expert, be skilled in somewhat different branches of the same department of knowledge. There must be in addition to these assistants provision for the execution of purely mechanical labor, for in shame be it spoken, fine minds before now have been ruined and fair bodies wrecked by being subjected to the iniquitous necessity of menial services which could just as well have been performed by minds and bodies of a much lower order.

Apparatus of various sorts, books and journals, collections of old material, access to new material, all come into the scheme. The division of labor is to be planned; criminal stunting of an assistant's growth by over-demands on his time or in routine work is to be avoided; instruction in the known and investigation of the unknown, but knowable, have to be arranged for. With successful organization, instruction and investigation go hand in hand, and students of the better sort, while acquiring existing knowledge, can add a necessary prop here or a new

beam there to the general mass of knowledge. There is no stimulus so great or so beneficial to good students as the feeling that by accurate, conscientious work they can contribute something, be it ever so little, to the world's store of facts. The time of medical students is usually so limited that only a few can possibly undertake long and complicated researches, but in a large laboratory, with the sort of organization I have in mind, a number of students working on a number of different points in one problem, each contributing his mite, can together collect a mass of data which, when integrated, make a contribution of no mean significance.

The anatomist, physiologist, or pathologist who directs his attention to the special study of neurological problems should, of course, have a solid foundation in general pathology and clinical medicine before giving himself over to such special studies. He should in connection with his work see autopsies, and, if possible, a certain number of patients, and should be in a position to consult with special workers in pathology and internal medicine, helping them, and in turn being helped by them. For in the study of the functions of the nervous system especially no stable conclusions have been or ever can be arrived at with regard to the higher groups of neurones, at least, without the rigid control of clinical and pathological observations on man. Morphologists working alone tend to become one-sided; isolated physiologists cannot fail to focus falsely, and the pathologist and the clinician, if out of touch with one another and with the students of normal structure and function, are bound to arrive at conclusions which are erroneous.

Let each one work by his own methods and push them as far as he can, but let each have reverence for and keep conversant with the work and results of others. We shall then have more facts and fewer hypotheses. Mindful of the fate of our speculative predecessors and in awe of the judgment of some scientific Dungara, we shall do best to make our sacrifices to the God of Things As They Are, rather than pay homage to the God of Things as They Should Be. In this way our building of knowledge will be slow, but what is lost in rapidity will be more than compensated for in solidity.

I have now done. From what I have said it will be clear to you that our knowledge of neurology, so slow in acquisition, is dependent upon the application of a large number of different methods of investigation differentiative and integrative. For the proper understanding of form relations the analyses require to be synthesized in particular and in general. Owing to the

special difficulties in solving problems in the nervous system and the increasing complexity of knowledge of structure and function and methods of investigation, co-operative activity is essential for progress. Such co-ordinated divided labor can be most satisfactorily performed in a series of well organized laboratories in association with medical schools, hospitals and asylums, and in connection with skilled clinical observers. The further pursuit of anatomical, physiological, chemical, pathological and clinical studies will permit of the recognition of ever increasing interrelations among the results with corresponding reciprocal benefit.